OCULAR PRESSURE REGULATION

Field of the Invention

This invention is directed to therapeutic methods and devices for the treatment of glaucoma. In particular, this invention is concerned with the use of a shunt or drain for the treatment of glaucoma. In another aspect this invention is concerned with ocular pressure spikes shunts and use of the same in ocular surgery.

Background of the Invention

The glaucomas are a common group of blinding conditions usuallyassociated with elevated intraocular pressure. This elevated pressure in the eye may be regarded as a disorder of the drainage system of the eye which gives rise to the glaucomas.

Aqueous humor of the eye ("aqueous") is a flowing liquid fluid (composed of sodium, chloride, bicarb, amino acids, glucose, ascorbic acid, and water) that is actively secreted by the ciliary body and flows out past the iris into the anterior chamber (are between the lens/iris and the cornea). The aquoeus drains out through angle formed by the iris and the sclera into a meshwork call the trabeculum, and from there into the canal of Schlem and then into the episcleral veins. Uveosclera drainage also occurs. Normal intraocular pressure (IOP) of aqueous in anterior chamber is between 10 and 20 mm Hg. Prolonged IOPs of greater than 21 mm Hg are associated with damage to optic nerve fibres.

In some cases of glaucoma the cause can be found: the trabecular meshwork becomes blocked by pigment or membrane. In other cases, blockage is due to a closure of the angle between the iris and the cornea. This angle type of glaucoma is referred to as "angle-closure glaucoma". In the majority of glaucoma cases, however, called "open angle glaucoma", the cause is unknown.

Elevated intraocular pressure results in the death of retinal ganglion cells (which convey retinal information to the brain) resulting in a characteristic pattern of loss of the field of vision, progressing to tunnel vision and blindness if left untreated.

Treatment of glaucoma consists predominantly of methods to lower the intraocular pressure (pharmacological, trabecular meshwork laser and surgery to drain fluid from the eye). More recently protection of the retinal ganglion cells by neuroprotective agents has been attempted.

Although pharmacological treatments of glaucoma have improved, they have important implications for the patient's quality of life, have compliance issues which are important in the elderly (in whom glaucoma is prevalent), expose the patient of glaucoma to side effects, and over a lifetime are costly.

Surgery for glaucoma treatment is usually a trabeculectomy in which a fistula is created to drain fluid from the anterior chamber to the subconjunctival space near the limbus, creating a bulge in the conjunctiva known as a bleb. Frequently scarring occurs and attempts to counter this with antimetabolites such as Mitomycin C have met with some success. In recalcitrant cases, glaucoma implants, drainage, shunt or valve devices have been developed eg Molteno (US Patent 4,457,757), Krupin (US Patent 5,454,746) and Baerveldt (US Patent 5,178,604). These suffer from similar problems of scarring (Classen L, Kivela T, Tarkkanen "A Histopathologic and immunohistochemical analysis of the filtration bleb after unsuccessful glaucoma seton implantation" *Am J Ophthalmol*, 1996;122:205-12) around the external opening of the tube devices in the subconjunctival space – the development of a large number of these devices is testament to the fact that many fail in the longer term. In these devices a drainage tube is located in the anterior chamber and is in fluid communication with the sclera or a surgically created subconjunctival space.

Whereas cataract surgery has been revolutionized in the last two decades, improvements in glaucoma surgery have been slower. Antifibrotic agents have improved the success rate of conventional filtration surgery (trabeculectomy), but with increased bleb leaks, blebitis, endophthalmitis and hypotensive maculopathy. Glaucoma shunts have had limited success in eyes that have "failed" multiple standard procedures. However complications with

malpositioned tubes, erosion & strabismus persist. A considerable issue is the lack of reproducibility and predictability in achieving the desired target intraocular pressure (IOP). Final IOP is largely determined by healing which can be unpredictable – in view of vast biological variations, it is impossible to predict which eyes will rapidly scar causing failure and which will fail to heal resulting in prolonged post-operative hypotony. Scarring remains a significant problem in all these external drainage proposals, where aqueous drains into the conjunctiva, or surgical chambers in the sclera.

The introduction of a new class of antiglaucoma drugs, the prostaglandin analogues has resulted in acknowledgment of the importance of the uveoscleral pathway in drainage of fluid form the eye (Hylton C, Robin AL "Update on prostaglandin analogs" *Curr Opin Ophthalmol*, 2003;14:65-9). Uveoscleral flow where aqueous humor flows through the interstitium of the ciliary muscle into the suprachoroidal space (a potential space between the choroids and sclera) and out through the sclera into the connective tissue of the orbit may account for 54% of outflow young healthy humans (Toris CB, Yablonski ME, Wang YL, Camras CB "Aqueous humor dynamics in the aging human eye" *Am J Ophthalmol*, 1999;127:407-12).

Cyclodialysis, the separation of the ciliary body from the scleral spur and underlying sclera, creates free communication between the anterior chamber and the suprachoroidal space and enhances uveoscleral flow. It has long been known that cyclodialysis can cause a profound reduction of intraocular pressure – initially (Fuchs E. "Detachment of the choroid inadvertently during cataract surgery" [German] *von Graefes Arch Ophthalmol*, 1900;51:199-224) cyclodialysis was recognized as a complication of cataract surgery. Deliberate creation of a cyclodialysis cleft for treating elevated intraocular pressure in uncontrolled glaucoma was first described as a surgical procedure in 1905 (Heine I. "Cyclodialysis, a new glaucoma operation" [German]) *Dtsch Med Wochenschr*, 1905;31:824-826. Since such clefts can heal and close spontaneously a number of devices have been used to keep them open, including platinum wire, horse hair, magnesium strips, tantalum foil, supramid, gelatin film, Teflon, silicone and polymethylmethacrylate (Rosenberg LF, Krupin T. "Implants in glaucoma surgery" Chapter 88, *The Glaucomas*,

Ritch R, Shields BM, Krupin T Eds. 2nd Edition Mosby St Louis 1986) and Hema (Mehta KR. "The suprachoroidal Hema wedge in glaucoma surgery" American Academy of Ophthalmology meeting 1977, pp 144). However the success rate of such approaches has been low (as low as 15%, Rosenburg & Krupin ibid and Gross RL, Feldman RM, Spaeth GL, *et al* "Surgical therapy of chronic glaucoma in aphakia and pseudophakia" *Ophthalmology*, 1988;95:1195-201). Failure was due to uncontrolled low pressure (hypotony) with consequentiqal macular edema, bleeding (hyphema) and inadequate pressure control.

The device and method of a first aspect of this invention takes advantage of the methods used in cataract surgery to develop a minimally invasive glaucoma procedure – thus small, self sealing incisions and materials that are biocompatible and fodable so that they fit through small openings will reduce surgical trauma and time. The controlled draining of aqueous into the suprachoroidal space according to this invention provides some predictability of outcome and overcomes scarring problems that have plagued glaucoma implants in the past.

The most frequent complication following modern cataract surgery with phacoemulsification, requiring specific treatment is elevated intraocular pressure (Cohen VM, Demetria H, Jordan K, Lamb RJ, Vivian AJ. :First day post-operative review following uncomplicated phacoemulsification" *Eye*, 1998;12 (Pt 4):634-6, and Dinakaran S, Desai SP, Raj PS. "Is the first post-operative day review necessary following uncomplicated phacoemulsification surgery?" *Eye*, 2000 Jun; 14 (Pt 3A):364-6. The increase may be marked and typically peaks at 5 to 7 hours before returning to near normal levels in 1 to 3 days (Hildebrand GD, Wickremasinghe SS, Tranos PG, Harris ML, Little BC. "Efficacy of anterior chamber decompression in controlling early intraocular pressure spikes after uneventful phacoemulsification" *J Cataract Refract Surg.*, 2003; 29:1087-92). Such pressure spikes can cause pain and may increase the risk of sight-threatening complications such as retinal vascular occlusion, increases loss of visual filed in advanced glaucoma and ischemic optic neuropathy – effects in otherwise healthy eyes are unknown (Hildebrand GD *et al*, ibid).

A number of prophylactic treatments are used with limited success – these include intacameral carbachol or acetylcholine, topical timolol, dorzolamide, aproclonidine, latanoprost and systemic acetazolamide (see Hildebrand GD *et al*, ibid). This also exposes the patient to the risk of drug side effects, increased cost and it has been postulated that reducing the flow of aqueous humor post surgery prolongs the residence time of bacteria that frequently (46.3% of cases) contaminate the anterior chamber during surgery (Srinivasan R, Tiroumal S, Kanungo R, Natarajan MK. "Microbial contamination of the anterior chamber during phacoemulsification" *J Cataract Refract Surg*, 2002; 28:2173-6.). This may increase the risk of endopthalmitis one of the most devastating sequeleae of intraocular surgery, since the bacteria are not being "flushed out" of the eye by the normal production of aqueous humour, the secretion of which has been suppressed by the drugs. Another technique is to decompress the anterior chamber by applying pressure to the posterior lip of the paracentesis wound at the appropriate time. This requires surveillance and could increase the risk of infection. Another aspect of this invention hereinafter described overcomes these problems.

Summary of the Invention

According to the present invention there is provided a flexible ocular device for implantation into the eye formed of a biocompatible elastomeric material, foldable to a diameter of 1.5 mm or less, comprising a fluid drainage tube having at one end a foldable plate adapted to locate the device on the inner surface of the sclera in a suprachoroidal space formed by cyclodialysis, said drainage tube opening onto the disc at one end and opening to the anterior chamber when implanted into the eye at its other end, so as to provide aqueous pressure regulation.

Preferably the fluid drainage tube has a diameter selected to provide predetermined resistance to aqueous humor flow, for example a pressure of 10 mm Hg or less. Alternatively said tube contains a valve so as to regulate pressure of the aqueous chamber at a predetermined level, for example at no less than 10 mm Hg.

In accordance with another embodiment of this invention there is provided a method for treating glaucoma which comprises:

providing a flexible ocular device formed of a biocomopatible elastomeric material foldable to a diameter of 1.5 mm or less, comprising a fluid drainage tube having at one end a foldable plate adapted to locate the device on the inner surface of the sclera and at its other end being open so as to allow fluid communication through said tube;

forming a small self-sealing incision at the juncture of the cornea and sclera of the eye opening into the anterior chamber;

filling the anterior chamber with a viscoelastic substance;

introducing the foldable ocular device into a suprachoroidal space formed by cyclodialysis via a hollow cannula, wherein said plate locates the device on the inner surface of the sclera in the suprachoroidal space, and said drainage tube is located in the anterior chamber of the eye so as to provide aqueous humor pressure regulation; and

thereafter removing said cannula and viscoelastic material from the eye.

In another aspect there is provided an ocular pressure spike shunt for insertion into an ocular paracentesis incision port following ocular surgery, comprising a flexible fluid transfer tube formed of biocompatible material, preferably biocompatible elastomeric material, so as to allow paracentesis incision closure around said tube, having an inner end and an outer end, a tubular lumen disposed between said inner end and said outer end to allow fluid communication through said tube, said lumen containing a valve for controlling pressure in the eye following ocular surgery, which valve opens permitting fluid flow through said tube when a predetermined pressure is exceeded, said shunt being configured such that on insertion into a paracentesis port said outer end is substantially flush with the surface of the cornea, and said inner end opens into the anterior chamber of the eye.

In another aspect there is provided a method for preventing ocular pressure spikes following ocular surgery wherein a paracentesis incision port is formed in the eye during said surgery, comprising introducing an ocular pressure spike shunt into said paracentesis port at the conclusion of ocular surgery, said shunt comprising a flexible fluid transfer tube formed of biocompatible material, preferably biocompatible elastomeric material, so as to

allow paracentesis incision closure around said tube, having an inner end and an outer end, a tubular lumen disposed between said inner end and said outer end to allow fluid communication through said tube, said lumen containing a valve for controlling pressure in the eye following ocular surgery, which valve opens permitting fluid flow through said tube when a predetermined pressure is exceeded, said shunt being configured such that on insertion into a paracentesis port said outer end is substantially flush with the surface of the cornea, and said inner end protrudes into the anterior chamber of the eye.

Description of the Figures

Figure 1 shows a diagrammatic representation of a side sectional view of suprachoroidal shunt insertion using an injector.

Figure 2 shows a diagrammatic representation of a side sectional view of an eye showing the unfolded plate portion of the device and a cannula introducing said device across the anterior chamber at 180° to the site of insertion.

Figure 3 shows a diagrammatic representation of an eye containing a pressure spike shunt inserted into a paracentesis port.

Detailed Description of the Preferred Embodiments of the Invention

The ocular device according to the present invention is implanted in a patient's eye using minimally invasive surgery techniques, adopted from modern cataract surgery.

The ocular device is formed from a biocompatible elastomeric material. Preferably, the device is made of soft surgical grade polymeric material, such as silicon or acrylic material such that the device is foldable and may be rolled up for insertion via a cannula. Figure 1 shows a proximal end of a cannula forming a cyclodialysis. The folded device may be introduced via such a cannula The elastomeric material is selected to be sufficiently soft that it does not erode delicate underlying choroid material when inserted into the eye. Such material and ocular lenses formed therefrom are well known and used in cataract surgery.

Sutures are not required to hold the device in place once surgically introduced into the eye, as the foldable plate is adapted to locate the device on the inner surface of the sclera in a suprachoroidal space formed by cyclodialysis (Figure 2). Preferably, the plate is of a disc-like shape which matches the curvature of the eye once unfolded. Figure 2 depicts an unfolded disc (connected tube not shown) after cannula introduction across the anterior chamber (transcameral). Alternatively, any plate-like configuration which locates the device on the inner surface of the sclera in the suprachoroidal space may be used, such as for example a rectangular foldable plate. Preferably the plate diameter is from 0.05 to 6 mm, and preferably the place thickness is from 12.5 μ to 250 μ. The fluid drainage tube of the ocular device is preferably integral with the plate, and is attached at one end to the plate, preferably at the periphery of the plate. Alternatively, the tube may be microwelded or otherwise fixed to the plate. Fabrication techniques well known in production of intraocular foldable lenses are preferably used in this invention. The tube has a hollow lumen, and is preferably of a length from about 1 mm to 4 mm. Preferred diameters of the tubing comprise an outer diameter of 400-1000 μ, and preferably the inner diameter is from 50 to 500 μ.

The diameter of the tube may be selected so as to provide a resistance to aqueous humor flow of predetermined pressure, preferably being a pressure less than 10 mm Hg. This enables the pressure of the aqueous to be regulated in a controlled manner, providing relief from excess ocular pressure associated with glaucoma, with avoidance of hypotony (uncontrolled low pressure). Alternatively, the tube may contain a valve, for example disposed at the end of the tube opening onto the disc so as to regulate ocular pressure at a predetermined level. Preferably, the valve prevents aqueous flow through the tube at a pressure of less than 10 mm Hg. Examples of valves which may be used include a slit valve. The drainage stops altogether if the pressure drops to a predetermined threshold level controlled by the valve.

The flexible foldable nature of the device according to the present invention enables well established techniques used in cataract surgery to be employed in the treatment of

glaucoma. The device according to the present invention may be folded into a cannula and introduced for location into the eye.

Intraocular surgery techniques allow a paracentesis (opening onto the anterior chamber from without at the juncture of the cornea and sclera – the limbus) to be performed and the anterior chamber filled with viscoelastic substance. A cyclodialysis instrument is introduced via the paracentesis, with the paracentesis preferably being carried out 180° from the insertion site. A cyclodialysis is carried out, for example by advancing an instrument tip into the angle between the ciliary body and sclera so as to create a cyclodialysis. This is preferably carried out with direct visualisation via gonioscopy lens viewed through an operating microscope. A surgical gonioscopy lens is preferably placed on the cornea while the cyclodialysis is carried out.

The rolled up ocular device is introduced through a cannula, for example using an introducer such as used in cataract surgery or other ocular surgery, from which the device can be detached by pressing a plunger into the introducer when the device has been inserted into the suprachoroidal space created by the cyclodialysis. The tubing of the device is positioned into the interior chamber, and the plate unfolds in the suprachoroidal space to locate the device in the eye. Because of its size, the device cannot fall through the opening through which it was introduced into the suprachoroidal space by the cyclodialysis. The plate therefore keeps the tube in the appropriate position in the anterior chamber allowing controlled aqueous drainage and providing an effective treatment for elevated ocular pressure.

The pressure spike shunt is designed to fit snugly in a paracentesis port that is routinely made during cataract or other ocular surgery. The tubing will not distort the port and there will be no leakage around the port. The outer end of the tube will sit flush on the surface of the cornea – the inner aspect of the tube will preferably just protrude into the anterior chamber – tube length will generally be 1-2 mm and tube diameter is preferably from 0.4-1.2 mm. The tube will contain the same valvular device as contained in the ocular device described above and will open when the intraocular pressure exceeds a predetermined

level, preferably10 mm Hg. At normal ocular pressure the valve will be closed, closing said tube to any fluid communication. Figure 3 shows a shunt located in a pareacentesis port. In most cases the shunt will be removed and discarded at the first post-operative dressing.

The shunt may be inserted into a paracentesis port, or one or more ports, using, for example, a punctum plug inserting instrument such as described in US Patent NO. 5,741,292.

This invention will now be described with reference to the following examples.

Example 1

Fresh whole porcine eyes were taken and mounted in a temperature controlled (37°) perfusion chamber. The eyes were perfused with Balanced Salt Solution via a 30 gauge needle inserted via a paracentesis into the anterior chamber. A peristaltic pump was used at a flow rate of 2 µl/min. Intraocular pressure was continuously monitored via a second paracentesis.

Typically intraocular pressures stabilized at 10-15 mm Hg and fell with time (the "washout effect", as glycosan aminoglycans are washed out of the trabecular meshwork with time). Creation of a cyclodialysis (initially with a small spatula, then viscoelastic injection to enlarge the area of detachment of the ciliary body from the sclera) with or without insertion of the device in the cyclodialysis cleft (silicone tubing, length 3mm, external diameter – 1 mm, plate diameter 3 mm) resulted in lower intraocular pressures (below 10 mm Hg) on reperfusion at the same perfusion rate as control eyes.

Example 2

Adequate anesthesia is provided to the eye of a glaucoma patient prepared for intraocular surgery. A paracentesis (opening into anterior chamber from without at the junction of the cornea and sclera – the limbus) is performed and the anterior chamber is filled with a viscoelastic substance. A surgical gonioscopy lens is placed on the cornea (or anterior

segment endoscope is used) and a cyclodialysis instrument is introduced via the paracentesis – the paracentesis is carried out 180° away from the planned implant insertion site. The cyclodialysis instrument tip is advanced into the angle and pushed into the space between the ciliary body and sclera creating a cycodialysis – this is carried out with direct visualization via the gonioscopy lens viewed through an operating microscope. In order to minimize bleeding, the area in the angle (anterior ciliary body face and overlying trabecular meshwork) can be lasered either preoperatively or at the time of surgery to abalate surface blood vessels).

Through an opening at the tip of the cyclodialysis instrument viscoelsatic is inserted to further create a space in the suprochoroidal space. The implant is then introduced – the device is rolled up in the same manner as an ultrathin intraocular lens. The ocular device is attached to an introducer from which it is detached by pushing a plunger in the introducer when the implant is inserted into the suprachoroidal space created by the cyclodialysis instrument and viscoelastic. The tubing is then positioned into the anterior chamber and may be cut to size. The plate unfolds in the suprachoroidal space and because of its size cannot fall throught the opening through which it was introduced into the suprachoroidal space. The plate therefore keeps the tube in an appropriate position. The valve is then flushed (with a cannula inserted via the paracentesis) via the tube opening in the anterior chamber. Viscoelastic is then removed from the anterior chamber and antibiotics, steroids and a dressing applied to the eye.

Example 3

Fresh whole porcine eyes were taken and mounted in a temperature controlled (37°) perfusion chamber as in Example 1. The eyes were perfused with Balanced Salt Solution via a 30 gauge needle inserted via a paracentesis into the anterior chamber. A peristaltic pump was used at a flow rate of 2 µl/min. Intraocular pressure was continuously monitored via a second paracentesis.

Typically intraocular pressures stabilized at 10-15 mmmHg and fell with time (the "washout effect, as glycoaminoglycans are washed out of the trabecular meshwork with

time). Silicone tubing, length 3 mm, external diameter 1 mm was introduced into one paracentesis port. One end of the port (outer end) was flush with the cornea and the inner end of the port extended slightly into the anterior chamber. Intraocular pressure did not exceed 10 mm Hg.

5